

CONFORMATIONAL ASSAYS TO DETECT BINDING TO G PROTEIN-COUPLED RECEPTORS

ABSTRACT OF THE DISCLOSURE

The present invention provides methods and compositions for detection of compounds that have activity in modulating G protein-coupled receptor (GPCR) activity, e.g., agonists, and antagonists. The detection method is based upon detection of a conformational change in a GPCR upon interaction with a ligand. Conformational change of the GPCR upon ligand interaction can be accomplished by modifying the GPCR to have a bound detectable label so that ligand interaction results in a conformational change in the GPCR that is detected by a change in detectable signal from the detectable label. Conformational change of the GPCR upon ligand interaction can also be detected by detecting a change in the accessibility of a protease cleavage site to protease cleavage, where the protease cleavage site is naturally-occurring in the GPCR or introduced into the GPCR. The conformational assays of the invention provide for high-throughput screening.

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